

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are respectfully requested.

By the foregoing amendment, claim 6 has been amended to be dependent upon claim 3. No new matter has been added.

Turning now to the Official Action, claim 6 has been objected to for being dependent upon a withdrawn claim. This objection is respectfully traversed. However, to expedite prosecution in the present application, and not to acquiesce to the Examiner's objection, applicants have hereby amended claim 6 so as to be dependent upon claim 3. Since the Examiner has indicated, on page 2 of the Official Action that "changing the dependency of claim 6 to claim 3 . . . would obviate this objection[,]" withdrawal of this objection is respectfully requested.

Claims 1-3, 6 and 9-14 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Goodman et al. (WO 98/27960) in view of Fleischer (1999, abstract only), or Fleischer (1999) and Miller et al. (1980, abstract only). This rejection is respectfully traversed.

The treatment of atopic dermatitis is very special and is not considered to be the same as or similar to the treatment of other skin diseases. In fact, the cause of atopic dermatitis has not been determined and, although some pharmaceutical compositions for the treatment of atopic dermatitis are on the market, an effective pharmaceutical composition for the treatment of atopic dermatitis has not been developed. An effective pharmaceutical composition for the treatment of atopic dermatitis has been strongly desired for many years. See page 1, line 20 to page 2,

line 25 of the present application. The present inventors, however, have discovered a very effective pharmaceutical composition for the treatment of atopic dermatitis.

WO '960 discloses a viscous hydrogel topical composition for treating inflamed skin, comprising an antimicrobially active nitroimidazol drug (see abstract). The nitroimidazol drug such as metroinidazole and tinidazole can be used in the topical treatment of certain dermatological diseases, including rosacea and eczema. In addition, various diseases to be treated by this composition are disclosed on page 1, lines 12 to 22. However, as admitted by the Examiner, WO '960 does not describe that the antimicrobially active nitroimidazol drug, *i.e.*, nitroimidazol drug such as metroinidazole and tinidazole, is effective for the treatment of atopic dermatitis.

Nonetheless, using improper hindsight reconstruction, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the inflamed skin diseases taught in WO '960 with atopic dermatitis in view of Fleischer (1999, abstract only), or Fleischer (1999) and Miller et al. (1980, abstract only).

The Examiner's allegations in this regard are not correct. That is, Fleischer describes "immune dysregulation appears to play an important role in the cause of atopic dermatitis," not as the Examiner indicates that immune regulation appears to play the important role.

Furthermore, Fleischer describes:

Topical corticosteroid agents have been the mainstay of therapy for atopic dermatitis because of their broad immunomodulatory effects. However, topical corticosteroid agents are not ideal agents because when used over the long term, they may cause cutaneous atrophy and immunosuppression.

That is, Fleischer clearly indicates that immune dysregulation appears to play an important role in the cause of atopic dermatitis and therefore, it has been believed that topical corticosteroid agents having broad immunomodulatory effects are effective for the treatment of atopic dermatitis. However, the topical corticosteroid agents are not good because they cause adverse effects such as immunosuppression.

Under such circumstances, Fleischer tried to find another effective agent for the treatment of atopic dermatitis, i.e., tacrolimus.

In this connection, Fleischer describes:

Systemic corticosteroidal agents, certain antihistaminic agents, systemic cyclosporine, and phototherapy have proven value in treating patients with atopic dermatitis. In the search for a noncorticosteroidal topical agent, tacrolimus stands out as being uniquely suited for this condition. Tacrolimus affects a broad spectrum of inflammatory mediators and processes known to be relevant to atopic dermatitis pathogenesis.

That is, Fleischer indicates that tacrolimus is an effective agent for the treatment of atopic dermatitis since tacrolimus affects a broad spectrum of inflammatory mediators and processes known to be relevant to atopic dermatitis pathogenesis. However, Fleischer never indicates that tacrolimus is an effective agent for the treatment of atopic dermatitis due to its immunosuppression activity. Furthermore, even though tacrolimus is an immunosuppressant, Fleischer never indicates or suggests that any immunosuppressant can be an effective agent for the treatment of atopic dermatitis.

It is impermissible to first ascertain factually what the inventors did and then view the prior art in such a manner as to select from the random facts of that art only those which may be modified and then utilized to reconstruct the inventors invention

from such prior art. See, e.g., *Panduit Corp. v. Dennison Mfg. Co.*, 227 U.S.P.Q. 337, 343 (Fed. Cir. 1985); *In re Shuman*, 227 U.S.P.Q. 54, 57 (C.C.P.A. 1966). For the reasons discussed above, one of ordinary skill in the art, at the time of applicants' invention, would not have viewed the claimed invention to have been taught or suggested by WO '962 taken together with Fleischer.

The Examiner argues, in the alternative, that applicants' claimed invention would have been obvious taking WO '962 in view of Fleischer and Miller. Miller, however, does not remedy the serious deficiencies of WO '962 in view of Fleischer.

Miller describes:

Two compounds, clotrimazole and dacarbaazine (DTIC) produced a dose related suppression of these responses. . . . whereas metronidazol and tinidazole actually enhanced the response It is suggested that experiments of this kind are helpful in identifying those imidazol compounds that could be used as immunosuppressants in vivo.

Therefore, Miller teaches experiments of this kind are helpful in identifying whether imidazol compounds can be used as immunosuppressant in vivo. Miller does not expressly teach that tinidazole can be used as an immunosuppressant in vivo.

Even if the Examiner is of the incorrect belief that Miller teaches that tinidazole can be used as an immunosuppressant in vivo, those skilled in the art would not have found the present invention obvious in view of this teaching since it is very difficult to treat atopic dermatitis and as discussed above atopic dermatitis is special. It is error for the Examiner to conclude that an invention is obvious on the grounds that "one might contemplate." Rather, the test under § 103 is whether the references, taken as a whole, would suggest the invention to one of ordinary skill in the art. See, e.g., *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 220 U.S.P.Q. 97, 110 (Fed. Cir. 1983). Here, the combination of references as set forth by the

Examiner fail to teach or suggest the claimed invention. Thus, a proper *prima facie* case of obviousness has not been established.

Assuming *arguendo* that a proper *prima facie* case of obviousness has been presented by the Examiner, it is well recognized that secondary considerations, such as unexpected results, may rebut the *prima facie* case of obviousness. The specification of the present application provides evidence of unexpected superior effects in the treatment of atopic dermatitis. For example, the present specification includes Test Examples 3 (pages 147-148), 4 (pages 148-150), 7 (pages 153-154), and 8 (pages 155-156) wherein ointments or creams containing tinidazole were used to treat atopic dermatitis demonstrate that the present invention produces such unexpected superior effects.

For all of the reasons discussed above, one of ordinary skill in the art would not have considered the claimed invention to have been taught or suggested by the prior art. Moreover, the unexpected superior results of the claimed invention rebut the Examiner's arguments concerning *prima facie* obviousness. As such, withdrawal of this rejection is respectfully requested.

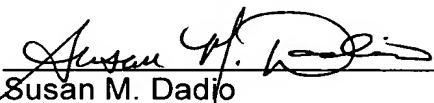
From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned attorney so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: May 17 2004

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